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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/887,540	06/21/2001	Robert Klein	R-193	5814
7590 10/21/2003				
DELTAGEN, INC. 1003 Hamilton Avenue Menlo Park, CA 94025			EXAMINER WILSON, MICHAEL C	
			ART UNIT 1632	PAPER NUMBER

DATE MAILED: 10/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/887,540	KLEIN, ROBERT	
	Examiner	Art Unit	
	Michael C. Wilson	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ____ MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 July 2003.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4 and 13-25 is/are pending in the application.
- 4a) Of the above claim(s) 1-4 and 13-16 is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 17-25 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____. | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The amendment to the description of Fig. 3A-3B has been entered.

This application contains claims 1-4 and 13-16 drawn to an invention nonelected with traverse in Paper No. 10. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claims 5-12 have been cancelled. Claims 17-25 have been added and are under consideration in the instant office action.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Applicant's arguments filed 7-30-03 have been fully considered but they are not persuasive.

This action is non-final in view of the new utility and art rejections below.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 17-25 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific or substantial asserted utility or a well-established utility.

Claims 17-19, 21-23 and 25 are directed toward a transgenic animal having a disruption of an LRP5 gene and retinal degeneration, increased anxiety or hypoactivity. The specification teaches making LRP5 $-/-$ mice (pg 50). The specification suggests using the mice to test compounds for neurological, neuropsychological or psychotic disease, but the specification does not disclose one specific neurological, neuropsychological or psychotic disease in humans linked to a disruption in LRP5 (pg 19, lines 8-11). The mice were tested in "open field testing" (Fig. 4 and 5 and pg 51); however, the results of the open field test do not correlate to a useful phenotype because "possible increased anxiety" and "significant hypoactivity" (lines 4 and 7 of pg 51) are not specific to any disease and are not statistically significant because the number of mice tested is not disclosed and the difference observed is not significant. In fact, it cannot be determined what the "2,1," means in "2,1, $-/-$, Male" or "2,1, $+/+$, Male" in Fig. 4 and 5. The mice also had retinal degeneration. The specification suggests using the mice as a model of disease relating to disruptions in LRP5 (pg 19, lines 4-6). However, retinal degeneration has not been linked to the LRP5 gene in humans. The mice claimed cannot be used to determine compounds that modulate LRP5 expression because LRP5 is not expressed in the mice. Using the mice to determining whether a particular phenotype is ameliorated is not a specific or substantial utility because the specification does not link the phenotype to any specific disease or to a disease caused by a disruption in humans. The specification does not identify any compounds that alter neurological, neuropsychological, or psychotic phenotypes using the mice. Thus, the

specification does not provide a specific or substantial use for a mouse having retinal degeneration, increased anxiety or hypoactivity as claimed.

Since the time of filing, LRP5 disruptions have been linked to osteoporosis-pseudoglioma syndrome (OPPG) in humans (Gong, 11-16-01, Cell, Vol. 107, pg 513-523, abstract), which is not taught or suggested in the instant application. A mouse having a homozygous disruption in LRP5 having features of osteoporosis-pseudoglioma syndrome has been made since the time of filing (Kato, J. Cell Biology, 2002, Vol.1 57, pg 303-314; abstract and pg 304, col. 2, "Generation of Lrp5^{-/-} mice"), which is not taught or suggested in the instant application.

Claim 24 is included because it is directed toward making the mouse, which lacks utility for reasons above. Claim 20, directed toward cells having a disrupted LRP5 gene, is included because the cells lack a specific and substantial utility for the reasons above and because the specification does not teach how to use the cells other than when they are part of a mouse that is a model of disease.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 17-25 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use mice having retinal degeneration, increased anxiety or hypoactivity.

In addition, claims 17 and 24 do not provide a nexus between the disruption in LRP5 and the lack of production of LRP5 or the phenotypes of retinal degeneration, increased anxiety or hypoactivity.

Claim 17 is directed toward a transgenic mouse having a disruption in LRP5 that lacks production of functional low density LRP5, and exhibits retinal degeneration, increased anxiety, or hypoactivity. Claim 24 is directed toward a method of making a transgenic mouse having a disruption in LRP5 using a mouse ES cell having a disruption in an endogenous LRP5 gene, introducing the cell into a mouse blastocyst, implanting the blastocyst into a pseudopregnant mouse which gives birth to chimeric mice, and breeding the chimeric mouse to produce the transgenic mouse, wherein the disruption is homozygous, the mouse lacks production of functional low density LRP5, and has retinal degeneration, increased anxiety, or hypoactivity.

The claims do not recite the disruption of LRP5 causes retinal degeneration, increased anxiety, or hypoactivity. In addition, increased anxiety and hypoactivity are relative terms and must be "relative to a wild-type mouse as in claim 18, for example. The specification does not teach disrupting the LRP5 gene in mice already lacking production of LRP5 or in mice already having retinal

degeneration. Given the unpredictability in the art of record taken with the guidance provided in the specification, the claim should reflect the teachings in the specification, which only teach mice having retinal degeneration as a result of LRP5 disruption. Otherwise, it would require one of skill undue experimentation to make the mouse as broadly claimed.

Claims 17-25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The amendment states support for the claims can be found on pg 8-15, 50 and 51. Such a statement is generic and does not support the claims as newly amended. For example, it cannot be found where a mouse having a disruption in LRP5 also has retinal degeneration as broadly claimed (claims 17 and 24). The specification only teaches a mouse having retinal degeneration as a result of a disruption in LRP5. The limitation of "increased anxiety", the specific phenotypes in claims 18, 19, 22 and 23, obtaining tissue (claim 20), heterozygous disruptions (claim 21) cannot be found.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 17-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 17 and 24 are indefinite because they do not clearly set forth that the disruption in LRP5 causes the lack of production of LRP5 or the retinal degeneration, increased anxiety or hypoactivity.

Claims 17 and 24 are indefinite because "increased anxiety and hypoactivity" are relative terms; however, the claims do not set forth to what the mice are being compared.

Claims 18 and 19 are indefinite because it is unclear whether the field test is related to the increased anxiety or hypoactivity in claim 17 or if it is in addition to the increased anxiety or hypoactivity in claim 17.

The term "characterized" in claims 18 and 19 is unclear. It cannot be determined if the claim is limited to the phenotype recited or if the claim encompasses mice having a phenotype related to the phenotype recited.

Claim 21 is indefinite because it cannot be determined if the mice have a homozygous or heterozygous disruption. While the claim states the mouse has a heterozygous disruption, the claim also requires "the disruption in the homozygous state".

The "increased anxiety" or "hypoactivity" in claims 22 and 23 lacks antecedent basis in claim 21.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 20 is rejected under 35 U.S.C. 102(b) as being anticipated by Weaver (J. Biol. Chem., 1997, Vol. 272, pg 14372-14379).

Weaver taught a mouse embryonic fibroblast having a disruption in LRP. The cell claimed does not require any particular phenotype. The cell of Weaver is equivalent to the cell claimed because the cell claimed has the same disruption and the same phenotype as the one taught by Weaver.

Double Patenting

Claim 25 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 17. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). The scope of the mouse in claim 25 is identical to the mouse in claim 17 because the method used to make the mouse of claim 25 does not impart any structural or functional difference in the mouse as compared to that of claim 17.

Conclusion

No claim is allowed.


Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached on Monday through Friday from 9:00 am to 5:30 pm at (703) 305-0120.

Questions of a general nature relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-1235.

If attempts to reach the examiner, patent analyst or Group receptionist are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051.

The official fax number for this Group is (703) 872-9306.

Michael C. Wilson



**MICHAEL WILSON
PRIMARY EXAMINER**